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VB

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/202,455	12/15/98	YAMAGUCHI K	FJN-070

HM22/1107

TESTA HURWITZ & THIBEAULT
125 HIGH STREET
HIGH STREET TOWER
BOSTON MA 02110

EXAMINER	
HAMUD,F	
ART UNIT	**PAPER NUMBER**
1647	13

DATE MAILED: 11/07/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File copy

Office Action Summary

Application No.	Applicant(s)
09/202,455	Yamaguchi et al
Examiner	**Group Art Unit**
Fozia Hamud	1647

☒ Responsive to communication(s) filed on *Aug 18, 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *65-92* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *65-92* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 1-64 have been canceled and new claims 65-59 have been added in Paper No.12 filed on August 18, 2000. Thus claims 65-59 are under consideration by the Examiner.

2. Receipt of Applicant's arguments and amendments filed in Paper No.12, 08/18/00 is acknowledged.

3. The following previous objections and rejections are withdrawn in light of Applicants amendments filed in Paper No.12, 08/18/00:

(I) Objection to the disclosure for missing abstract.

(ii) Objection to the disclosure for not referencing the PCT Application.

(iii) Objection to the disclosure for reciting the word "novel" in the title.

(iv) All the outstanding rejections of claims 1-64 are withdrawn in view of the cancellation of claims 1-64.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Applicant's arguments filed in Paper No.12, 08/18/00, have been fully considered but were deemed persuasive in part. The issues remaining are restated below.

6. ***Priority Dates:***

a) 09 7808/1997 filed on 04/15/97 discloses osteoclastogensis inhibitory factor binding molecule (OBM) produced by mouse osteoblast stromal cell line ST2, therefore, only claims to OCIF binding molecule purified from natural resources would get this priority date.

b) 151434/1997 filed on 06/09/97 discloses mouse cDNA encoding OCIF binding molecule, and the full length mouse protein sequence. Claims drawn to mouse DNA and encoded protein get this priority date.

c) 217897/1997 filed on 08/12/97 discloses fragments of the mouse OBM 72-316, 76-316.

d) 224803/97 filed on 08/21/97 discloses human cDNA and encoded protein and fragments thereof. Claims to human DNA and encoded protein get this priority date.

Claim objections

7. Claim 73 and 77 are objected to because of the following informalities:

claim 73 is objected to, because it has a spelling error. In line 2, the word "domane" should be replaced by "domain".

Claim 77 is objected to as using improper/incomplete Markush language. (See M.P.E.P. 706.03(y).) Applicants should delete the use of "or" in line 3, with the last alternative embodiment and substitute "and" instead.

Claim Rejections - 35 USC § 112

8. Claims 65-76, 77-81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated mouse osteoclastogensis inhibitory (OCIF) binding protein comprising the amino acid sequence set forth in SEQ ID NO:1 and an isolated human OCIF binding protein comprising the amino acid sequence set forth in SEQ ID NO:11, said polypeptide encoded by a polynucleotide comprising the nucleotide sequence set forth in SEQ ID NO:2 or SEQ ID NO:12 respectively, and a fragment of the polypeptide of SEQ ID NO:1 comprising amino acid residues 72-316 or 76-316, and a method of recombinantly making

said polypeptides, is not enabling for "all" possible mouse or human purified osteoclastogensis inhibitory (OCIF) binding proteins, or "all" soluble, membrane proteins, or secreted mouse or human purified OCIF binding proteins, or "all" human or mouse OCIF binding proteins that lack the transmembrane domain or that are fused to a heterologous protein sequence, or fragments, analogs or variants of said proteins that bind to OCIF or promote osteoclast differentiation and maturation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 64 recites "a purified and isolated OCIF binding protein...", what is claimed in claim 64 broadly encompasses "all" proteins that bind to OCIF, while the specification discloses that the mouse polypeptide comprising the amino acid sequence set forth in SEQ ID NO:1 and the human polypeptide comprising the amino acid sequence set forth in SEQ ID NO:11 are proteins produced recombinantly or produced and purified from osteoblastic stromal cells, that bind to labeled OCIF, comprise apparent molecular weight of 30,000 to 40,000 Daltons and promote osteoclast differentiation and maturation (see pages 53, 67 and 85, 108 and Figures 1, 2, and 26). The specification further discloses that the OCIF binding protein of the instant invention can be membrane bound or in a solubilized form. However, the specification is non-enabling for the unlimited number of proteins having OCIF binding property which are encompassed by the scope of the claims. Also the instant specification is non-enabling for all human and mouse proteins that exhibit activity promoting osteoclast differentiation and maturation as recited in claim 6.

With respect to claims 70-71 which recite fragments of OCIF binding protein, the only fragments enabled by the instant specification are the fragments comprising amino acid residues 72-316 or 76-316 of the polypeptide of SEQ ID NO:1, and not "all" possible fragments as recited in the claims, the specification does not provide the requisite examples nor a representative number of different sequences that would allow the skilled artisan to produce fragment of the polynucleotide of SEQ ID NO:1 or 11 which retains it's ability to bind to OCIF.

With respect to claims 77 and 81, instant specification is non-enabling for polypeptide encoded by a nucleic acid sequence which hybridizes to the complement of SEQ ID NO:2, 12, 15, 18 or 19, at the conditions recited in the claims, said polypeptide retaining its OCIF binding property, because instant specification does disclose said polypeptide. Instant specification only discloses a polypeptide encoded by the polynucleotides of SEQ ID NO:2, 12, 15, 18 or 19, however, there is no teaching or guidance that a nucleic acid sequence which hybridizes to the complement of SEQ ID NO:2, 12, 15, 18 or 19 would encode a polypeptide that binds to OCIF. Furthermore, in the absence of a sufficient number of examples to enable the scope of the claims, the specification fails to provide the necessary guidance with assurance that one of ordinary skill in the art would obtain the products that possess the desired properties. With respect to claims 70-71, which recite "...a fragment, analog or variant of the OCIF binding protein...), the specification does not disclose any analogs or variants of the polypeptides of SEQ ID NO:1 or 11. In the specification (pages 15-30), Applicants describe the isolation, expression and sequence determination of cDNAs encoding human and mouse proteins which specifically bind to OCIF. However, there is no disclosure of any variants or analogs of the human or mouse polypeptide.

There is no guidance in the specification as to how one of ordinary skill in the art would generate a polynucleotide or a polypeptide encoded thereby, other than that exemplified. The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant case, the issue is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. The instant claims are not limited to naturally-occurring compounds and the instant specification does not provide a description of a repeatable process of producing a fragment, an analog or a variant of the polypeptide of SEQ ID NO:1 or 11, which retains the ability to bind to OCIF. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of those nucleotide of the disclosed naturally-occurring polynucleotide, which are required to encode a functional protein. It is this additional characterization of the disclosed polynucleotide that is required in order to obtain the functional and structural data needed to permit one to produce a polypeptide which meets both the structural and functional requirements of the instant claim that constitutes undue experimentation.

Therefore Applicants have not presented enablement commensurate in scope with the claims 65-81.

8b. Claims 70-71 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only discloses the isolated protein comprising the amino acid sequence set forth in SEQ ID NO:1 or 11, and therefore the written description is not commensurate in scope with the claims drawn to variants or analogues of the protein with the amino acid sequence set forth of SEQ ID NO:1 or 11 as recited in claims 70-71.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of

that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO: NO:1 and 11, the skilled artisan cannot envision the detailed structure of the encompassed polypeptide or the polynucleotide encoding such and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Applicants describe the isolation, expression and sequence determination of human and mouse proteins which specifically bind to OCIF. However, there is no disclosure of variants or analogs of the mouse or human protein comprising the amino acid sequence set foeth in SEQ ID NO:1 or 11.

Therefore only isolated polypeptide comprising the amino acid sequence of SEQ ID NO:1, or 11, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. 112, first paragraph. As a result, it does not appear that the inventors were in possession of variants or analogues or fragments (with the exception of the fragment comprising amino acid residues 72-316 or 76-316 of the polypeptide of SEQ ID NO:1), of the polypeptides of SEQ ID NO:1 or 11.

9a. Claims 64-76, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9b. Claims 64-79, 81-85-91 are vague and indefinite for reciting the acronym "OCIF....", because this acronym is not descriptive of the claimed protein, furthermore, more than one protein can be known by the same acronym. Reciting the full name of the protein in the first independent claim would obviate this rejection. Appropriate correction is required.

9b. Claim 83 is vague and indefinite for the recitation of "...said fragment is about 690 bp....", which renders the claim unclear because "about" indefinite, should the fragment be 600 bp, 500 bp, 1000 bp or something else?. The metes and bounds of the claim is not ascertainable.

Claim Rejections - 35 U.S.C. § 102

10 a. Claims 69, 72, 77-81, 85-91 are rejected under 35 U.S.C. 102(e) as being anticipated by Boyle (US Patent 5,843,678) for the same reason as canceled claims 1, 8-16, 21-31, 36, 39-41, 43-44, see office action mailed on 2/25/00 in Paper No.10, pages 12-14.

Boyle teaches an isolated murine nucleic acid molecule encoding a protein, that specifically binds to osteoprotegrin (OPG), an expression vector comprising said nucleic acid molecule and a method of making the encoded protein, (see column 3, lines 15-60, and Example 2). The protein disclosed by Boyle comprises 316 amino acid in length, has amino acid terminal, cytoplasmic domain, a transmembrane domain and a carboxyl terminal extracellular domain, and is involved in osteoclast differentiation, (see column 2, lines 20-55). The OPG binding protein disclosed by Boyle may be membrane-associated or may be in soluble form.

The polynucleotide disclosed by Boyle shares 100% identity to instantly claimed polynucleotide sequence of SEQ ID NO: 2, and encodes a polypeptide which shares 100% identity to the polypeptide of SEQ ID NO:1 of the present invention. Therefore Boyle's reference clearly anticipates the instant claims 1, 8-16, 21-31, in the absence of any evidence to the contrary. Applicant's earliest effective priority for mouse polypeptide of SEQ ID NO:1 encoded by SEQ ID NO:2, is to document 151434/1997 filed on 06/09/97, which discloses mouse cDNA encoding OCIF binding molecule, and the full length mouse protein sequence. Therefore, claims drawn to mouse polynucleotide of SEQ ID NO:2 encoding the polypeptide of SEQ ID NO:1, and recombinant production of said polypeptide get the benefit of this priority date (i.e 06/09/97). Applicants argue that their earliest effective priority is to Japanese Patent Application 97808/1997 filed on 04/15/97, however, this document discloses only osteoclastogensis inhibitory factor binding molecule (OBM) produced by mouse osteoblast stromal cell line ST2, and it discloses no sequences, therefore, claims drawn to isolated polypeptide of SEQ ID NO:1 encoded by SEQ ID NO:2, would not get the benefit of this priority date.

With respect to claims 77 and 81 the polynucleotide of Boyle would be expected to hybridize completely to the complement of instant claimed polynucleotide of SEQ ID NO:2, 15 or 18 under any hybridization conditions, and encode a polypeptide that binds to OCIF.

New Rejections:

10 b. Claims 69, 72-81, 85-91 are rejected under 35 U.S.C. 102(e) as being anticipated by Anderson et al (US Patent 6,017,729).

Anderson et al teach an isolated human nucleic acid molecule encoding an isolated polypeptide that comprises 317 amino acid residues, (see column 2, lines 1-45). The protein disclosed by Anderson et al comprises 317 amino acid in length, has amino acid terminal, cytoplasmic domain, a transmembrane domain and a carboxyl terminal extracellular domain, is prepared in a soluble form or membrane bound form, (see column 2, lines 1-45).

The polynucleotide disclosed by Anderson et al shares 100% identity to instantly claimed polynucleotide sequence of SEQ ID NO: 12, and 19, and encodes a polypeptide which shares 100% identity to the polypeptide of SEQ ID NO:11and 17 of the present invention. See attached copies of the comparison of SEQ ID NO:19 and SEQ ID NO:17 claimed in the instant invention and the sequences of the reference (SEQUENCE COMPARISON 'A' and 'B', respectively). Therefore Anderson's reference clearly anticipates the instant claims 69, 72-81, 85-91, in the absence of any evidence to the contrary. Applicant's earliest effective priority for human polypeptide of SEQ ID NO:11, and 17 encoded by SEQ ID NO:12 and 19, respectively, is to document 224803/97 filed on 08/21/97, which discloses human cDNA and encoded protein and fragments thereof. Therefore, claims drawn to human polynucleotide of SEQ ID NO:12 or 19 encoding the polypeptide of SEQ ID NO:11 or 17, respectively, and recombinant production of said polypeptide get the benefit of this priority date (i.e 08/21/97).

With respect to claims 77 and 81 the polynucleotide disclosed in the Anderson et al reference would be expected to hybridize completely to the complement of instant claimed polynucleotide of SEQ ID NO:12, or 19 under any hybridization conditions.

10 c. Claims 82 and 83 are rejected under 35 U.S.C. 102(b) as being anticipated by Anderson et al (11/97).

Anderson et al reference discloses a nucleotide sequence that shares 100% homology to the nucleotide sequence of SEQ ID NO:6 and 9 of the instant application, (SEQUENCE COMPARISON 'C' and 'D'). The polynucleotide disclosed by Anderson et al meets the fragment limitation recited in claims 82 and 83, therefore, this reference anticipates claims 82 and 83.

Conclusion

11. No claim is allowable.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8896. The examiner can normally be reached on Monday-Friday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
November 02, 2000

Gary L. Kunz
GARY L. KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Sequence Comparison A

Query Match 100.0%; Score 1301; DB 3; Length 317;
Best Local Similarity 100.0%; Pred. No. 9.7e-139;
Matches 246; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy    241 KVRDID 246
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Db    312 KVRDID 317
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RESULT 2
US-08-996-139-11
; Sequence 11, Application US/08996139
; Patent No. 6017729
; GENERAL INFORMATION:
; APPLICANT: Anderson, Dirk M.
; APPLICANT: Galibert, Laurent
; APPLICANT: Maraskovsky, Eugene
; TITLE OF INVENTION: Receptor Activator of NF-kappaB
; NUMBER OF SEQUENCES: 19
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Immunex Corporation, Law Department
; STREET: 51 University Street
; CITY: Seattle
; STATE: WA
; COUNTRY: USA
; ZIP: 98101
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: Apple Power Macintosh
; OPERATING SYSTEM: Apple Operating System 7.5.5
; SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/996,139
; FILING DATE: 22 DECEMBER 1997
; CLASSIFICATION:
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: USSN 60/064,671
; FILING DATE: 14 OCTOBER 1997
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: USSN 08/813,509
; FILING DATE: 07 MARCH 1997
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: USSN 08/772,330
; FILING DATE: 23 DECEMBER 1996
; ATTORNEY/AGENT INFORMATION:
; NAME: Perkins, Patricia Anne
; REGISTRATION NUMBER: 34,693
; REFERENCE/DOCKET NUMBER: 2851-A
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (206)587-0430
; TELEFAX: (206)233-0644
; INFORMATION FOR SEQ ID NO: 11:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 294 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
; MOLECULE TYPE: protein

US-08-996-139-11

Query Match 85.8%; Score 1116; DB 3; Length 294;
Best Local Similarity 85.0%; Pred. No. 6.7e-118;
Matches 209; Conservative 14; Mismatches 21; Indels 2; Gaps 1;

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Qy    121 GWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVTKTSIKIPS 180
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Qy    241 KVRDID 246
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Db    289 KVQDID 294
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RESULT 3
US-08-842-842-7
; Sequence 7, Application US/08842842
; Patent No. 5843678
; GENERAL INFORMATION:
; APPLICANT: Boyle, William J.
; TITLE OF INVENTION: OSTEOPROTEGERIN BINDING PROTEINS
; NUMBER OF SEQUENCES: 7
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Amgen Inc.
; STREET: 1840 Dehavilland Drive
; CITY: Thousand Oaks
; STATE: California
; COUNTRY: USA
; ZIP: 91230-1789
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.30
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/842,842
; FILING DATE:
; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: Winter, Robert B.
; REFERENCE/DOCKET NUMBER: A-451
; INFORMATION FOR SEQ ID NO: 7:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 316 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
; MOLECULE TYPE: protein
US-08-842-842-7

Query Match 85.2%; Score 1109; DB 2; Length 316;
Best Local Similarity 84.6%; Pred. No. 4.7e-117;
Matches 208; Conservative 14; Mismatches 22; Indels 2; Gaps 1;

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Qy     61 QHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSHKVSLSSWYHDR 120
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GenCore version 4.5

OM protein - protein search, using sw model

Run on: November 1, 2000, 14:55:50 ; Search time 54.03 Seconds
(without alignments)
76.314 Million cell updates/sec

Title: US-09-202-455-17
Perfect score: 1301
Sequence: 1 AQMDPNRISEDGTHCIYRIL.....LLDPDQDATYFGAFKVRDID 246

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 164575 seqs, 16761186 residues

Total number of hits satisfying chosen parameters: 164575

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : Issued_Patents_AA:*
1: /cgn2_6/ptodata/1/iaa/5A_COMB.pep:*
2: /cgn2_6/ptodata/1/iaa/5B_COMB.pep:*
3: /cgn2_6/ptodata/1/iaa/6_COMB.pep:*
4: /cgn2_6/ptodata/1/iaa/PCTUS_COMB.pep:*
5: /cgn2_6/ptodata/1/iaa/backfiles1.pep:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	1301	100.0	317	3	US-08-996-139-13	Sequence 13, Appl
2	1116	85.8	294	3	US-08-996-139-11	Sequence 11, Appl
3	1109	85.2	316	2	US-08-842-842-7	Sequence 7, Appli
4	235.5	18.1	281	1	US-08-670-354-2	Sequence 2, Appli
5	235.5	18.1	281	3	US-08-584-031-1	Sequence 1, Appli
6	235.5	18.1	281	3	US-08-780-496-1	Sequence 1, Appli
7	235.5	18.1	281	4	PCT-US96-10895-2	Sequence 2, Appli
8	235	18.1	291	1	US-08-670-354-6	Sequence 6, Appli
9	235	18.1	291	4	PCT-US96-10895-6	Sequence 6, Appli
10	164.5	12.6	376	3	US-08-751-512-8	Sequence 8, Appli
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14	150	11.5	261	1	US-08-184-422-8	Sequence 8, Appli
15	150	11.5	261	1	US-08-360-923A-2	Sequence 2, Appli
16	150	11.5	261	1	US-08-446-922-4	Sequence 4, Appli
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18	150	11.5	261	2	US-08-690-096-2	Sequence 2, Appli
19	150	11.5	261	2	US-08-249-189-12	Sequence 12, Appl
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21	150	11.5	261	2	US-08-477-733B-12	Sequence 12, Appl
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37	149.5	11.5	281	3	US-08-815-190A-2	Sequence 2, Appli
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39	145.5	11.2	145	3	US-08-630-172-5	Sequence 5, Appli
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43	141	10.8	158	1	US-07-794-400-6	Sequence 6, Appli
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ALIGNMENTS

Sequence Comparison 'A'

RESULT 1
US-08-996-139-13
; Sequence 13, Application US/08996139
; Patent No. 6017729
; GENERAL INFORMATION:
; APPLICANT: Anderson, Dirk M.
; APPLICANT: Galibert, Laurent
; APPLICANT: Maraskovsky, Eugene
; TITLE OF INVENTION: Receptor Activator of NF-kappaB
; NUMBER OF SEQUENCES: 19
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Immunex Corporation, Law Department
; STREET: 51 University Street
; CITY: Seattle
; STATE: WA
; COUNTRY: USA
; ZIP: 98101
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: Apple Power Macintosh
; OPERATING SYSTEM: Apple Operating System 7.5.5
; SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/996,139
; FILING DATE: 22 DECEMBER 1997
; CLASSIFICATION:
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: USSN 60/064,671
; FILING DATE: 14 OCTOBER 1997
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: USSN 08/813,509
; FILING DATE: 07 MARCH 1997
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: USSN 08/772,330
; FILING DATE: 23 DECEMBER 1996
; ATTORNEY/AGENT INFORMATION:
; NAME: Perkins, Patricia Anne
; REGISTRATION NUMBER: 34,693
; REFERENCE/DOCKET NUMBER: 2851-A
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (206)587-0430
; TELEFAX: (206)233-0644
; INFORMATION FOR SEQ ID NO: 13:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 317 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
; MOLECULE TYPE: protein
US-08-996-139-13

See over

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;    ANTI-SENSE:  NO
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;    IMMEDIATE SOURCE:
;      LIBRARY:
;      CLONE:  huRANKL (full length)
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;      NAME/KEY:  CDS
;      LOCATION:  1..951
US-08-996-139-12
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RESULT   2
US-08-996-139-10
; Sequence 10, Application US/08996139
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; Patent No. 6017729
;  GENERAL INFORMATION:
;    APPLICANT:  Anderson, Dirk M.
;    APPLICANT:  Galibert, Laurent
;    APPLICANT:  Maraskovsky, Eugene
;    TITLE OF INVENTION:  Receptor Activator of NF-kappaB
;    NUMBER OF SEQUENCES:  19
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Immunex Corporation, Law Department
;      STREET:  51 University Street
;      CITY:  Seattle
;      STATE:  WA
;      COUNTRY:  USA
;      ZIP:  98101
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  Apple Power Macintosh
;      OPERATING SYSTEM:  Apple Operating System 7.5.5
;      SOFTWARE:  Microsoft Word for Power Macintosh 6.0.1
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/996,139
;      FILING DATE:  22 DECEMBER 1997
;      CLASSIFICATION:
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  USSN 60/064,671
;      FILING DATE:  14 OCTOBER 1997
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  USSN 08/813,509
;      FILING DATE:  07 MARCH 1997
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  USSN 08/772,330
;      FILING DATE:  23 DECEMBER 1996
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Perkins, Patricia Anne
;      REGISTRATION NUMBER:  34,693
;      REFERENCE/DOCKET NUMBER:  2851-A
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (206)587-0430
;      TELEFAX:  (206)233-0644
;  INFORMATION FOR SEQ ID NO:  10:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  1630 base pairs
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;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  cDNA
;    HYPOTHETICAL:  NO
;    ANTI-SENSE:  NO
;    ORIGINAL SOURCE:
;      ORGANISM:  Mus musculus
;    IMMEDIATE SOURCE:
;      LIBRARY:
;      CLONE:  RANKL
;    FEATURE:
;      NAME/KEY:  CDS
;      LOCATION:  3..884
US-08-996-139-10
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Scoring table: IDENTITY_NUC
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Searched: 262060 seqs, 75620727 residues

Total number of hits satisfying chosen parameters: 524120

Minimum DB seq length: 0
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Post-processing: Minimum Match 0%
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Listing first 45 summaries

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Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

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	44	28.6	3.9	9890	1	US-08-232-463-18	Sequence 18, Appl
	45	28.4	3.8	52	3	US-08-842-842-1	Sequence 1, Appli

ALIGNMENTS

Sequence Comparison B

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US-08-996-139-12
; Sequence 12, Application US/08996139
; Patent No. 6017729
; GENERAL INFORMATION:
; APPLICANT: Anderson, Dirk M.
; APPLICANT: Galibert, Laurent
; APPLICANT: Maraskovsky, Eugene
; TITLE OF INVENTION: Receptor Activator of NF-kappaB
; NUMBER OF SEQUENCES: 19
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Immunex Corporation, Law Department
; STREET: 51 University Street
; CITY: Seattle
; STATE: WA
; COUNTRY: USA
; ZIP: 98101
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: Apple Power Macintosh
; OPERATING SYSTEM: Apple Operating System 7.5.5
; SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/996,139
; FILING DATE: 22 DECEMBER 1997
; CLASSIFICATION:
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: USSN 60/064,671
; FILING DATE: 14 OCTOBER 1997
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: USSN 08/813,509
; FILING DATE: 07 MARCH 1997
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: USSN 08/772,330
; FILING DATE: 23 DECEMBER 1996
; ATTORNEY/AGENT INFORMATION:
; NAME: Perkins, Patricia Anne
; REGISTRATION NUMBER: 34,693
; REFERENCE/DOCKET NUMBER: 2851-A
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (206)587-0430
; TELEFAX: (205)233-0644
; INFORMATION FOR SEQ ID NO: 12:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 954 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; MOLECULE TYPE: cDNA

See over

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          Japan (E-mail:YSNT@t-cnet.or.jp, Tel:81-285-52-2821,
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Matches 22; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Sequence Comparison C'

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DEFINITION  Mus musculus receptor activator of nuclear factor kappa B ligand
            (RANKL) mRNA, complete cds.
ACCESSION   AF019048
VERSION     AF019048.1  GI:2612923
KEYWORDS    .
SOURCE      house mouse.
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1  (bases 1 to 2225)
  AUTHORS   Anderson,D.M., Maraskovsky,E., Billingsley,W.L., Dougall,W.C.,
            Tometsko,M.E., Roux,E.R., Teepe,M.C., DuBose,R.F., Cosman,D. and
            Galibert,L.
  TITLE     A homologue of the TNF receptor and its ligand enhance T-cell
            growth and dendritic-cell function
  JOURNAL   Nature 390 (6656), 175-179 (1997)
  MEDLINE   98032977
REFERENCE   2  (bases 1 to 2225)
  AUTHORS   Anderson,D.M., Billingsley,W., Dougall,W., Maraskovsky,E.,
            Cosman,D., DuBose,R. and Galibert,L.
  TITLE     Direct Submission
  JOURNAL   Submitted (13-AUG-1997) Molecular Biology, Immunex Corp., 51
            University St., Seattle, WA 98101, USA
FEATURES             Location/Qualifiers
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BASE COUNT      623 a    468 c    523 g    611 t
ORIGIN
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Query Match 100.0%; Score 22; DB 12; Length 2225;
Best Local Similarity 100.0%; Pred. No. 0.2;
Matches 22; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Db   1064 AAGCCCCAAAGTACGTCGCATC 1043
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RESULT   7
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LOCUS       AF013170     2237 bp    mRNA            ROD       05-NOV-1998
DEFINITION  Mus musculus TNF-related ligand TRANCE mRNA, complete cds.
ACCESSION   AF013170
VERSION     AF013170.1  GI:2411497
KEYWORDS    .
SOURCE      house mouse.
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1  (bases 1 to 2237)
  AUTHORS   Wong,B.R., Rho,J., Arron,J., Robinson,E., Orlinick,J., Chao,M.,
            Kalachikov,S., Cayani,E., Bartlett,F.S. III, Frankel,W.N., Lee,S.Y.
            and Choi,Y.
  TITLE     TRANCE is a novel ligand of the tumor necrosis factor receptor
            family that activates c-Jun N-terminal kinase in T cells
  JOURNAL   J. Biol. Chem. 272 (40), 25190-25194 (1997)
  MEDLINE   97460112
REFERENCE   2  (bases 1 to 2237)
  AUTHORS   Wong,B.R., Josien,R., Lee,S.Y., Sauter,B., Li,H.L., Steinman,R.M.
            and Choi,Y.
  TITLE     TRANCE (tumor necrosis factor [TNF]-related activation-induced
            cytokine), a new TNF family member predominantly expressed in T
            cells, is a dendritic cell-specific survival factor
  JOURNAL   J. Exp. Med. 186 (12), 2075-2080 (1997)
  MEDLINE   98060869
REFERENCE   3  (bases 1 to 2237)
  AUTHORS   Fuller,K., Wong,B., Fox,S., Choi,Y. and Chambers,T.J.
  TITLE     TRANCE is necessary and sufficient for osteoblast-mediated
            activation of bone resorption in osteoclasts
  JOURNAL   J. Exp. Med. 188 (5), 997-1001 (1998)
  MEDLINE   98401035
REFERENCE   4  (bases 1 to 2237)
  AUTHORS   Wong,B.R., Josien,R., Lee,S.Y., Vologodskaia,M., Steinman,R.M. and
            Choi,Y.
  TITLE     The TRAF family of signal transducers mediates NF-kappaB activation
            by the TRANCE receptor
  JOURNAL   J. Biol. Chem. 273 (43), 28355-28359 (1998)
  MEDLINE   98447691
REFERENCE   5  (bases 1 to 2237)
  AUTHORS   Wong,B.R., Rho,J., Arron,J., Lee,S.Y., Robinson,E. and Choi,Y.
  TITLE     Direct Submission
  JOURNAL   Submitted (09-JUL-1997) Howard Hughes Medical Institue, The
            Rockefeller University, 1230 York Ave., New York, NY 10021, USA
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ORIGIN


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RESULT   6
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DEFINITION  Mus musculus receptor activator of nuclear factor kappa B ligand
            (RANKL) mRNA, complete cds.
ACCESSION   AF019048
VERSION     AF019048.1  GI:2612923
KEYWORDS    .
SOURCE      house mouse.
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1  (bases 1 to 2225)
  AUTHORS   Anderson,D.M., Maraskovsky,E., Billingsley,W.L., Dougall,W.C.,
            Tometsko,M.E., Roux,E.R., Teepe,M.C., DuBose,R.F., Cosman,D. and
            Galibert,L.
  TITLE     A homologue of the TNF receptor and its ligand enhance T-cell
            growth and dendritic-cell function
  JOURNAL   Nature 390 (6656), 175-179 (1997)
  MEDLINE   98032977
REFERENCE   2  (bases 1 to 2225)
  AUTHORS   Anderson,D.M., Billingsley,W., Dougall,W., Maraskovsky,E.,
            Cosman,D., DuBose,R. and Galibert,L.
  TITLE     Direct Submission
  JOURNAL   Submitted (13-AUG-1997) Molecular Biology, Immunex Corp., 51
            University St., Seattle, WA 98101, USA
FEATURES             Location/Qualifiers
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                     AQPFAHLTINAASIPSGSHKVTLSSWYHDRGWAKISNMTLSNGKLRVNQDGFYYLYAN
                     ICFRHHETSGSVPTDYLQLMVYVVKTSIKIPSSHNLMKGGSTKNWSGNSEFHFYSINV
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BASE COUNT      623 a    468 c    523 g    611 t
ORIGIN


  Query Match             100.0%;  Score 20;  DB 12;  Length 2225;
  Best Local Similarity   100.0%;  Pred. No. 1.3;
  Matches   20;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 atcagaagacagcactcact 20
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Db    376 ATCAGAAGACAGCACTCACT 395


RESULT   7
AF013170
LOCUS       AF013170     2237 bp    mRNA            ROD       05-NOV-1998
DEFINITION  Mus musculus TNF-related ligand TRANCE mRNA, complete cds.
ACCESSION   AF013170
VERSION     AF013170.1  GI:2411497
KEYWORDS    .
SOURCE      house mouse.
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1  (bases 1 to 2237)
  AUTHORS   Wong,B.R., Rho,J., Arron,J., Robinson,E., Orlinick,J., Chao,M.,
            Kalachikov,S., Cayani,E., Bartlett,F.S. III, Frankel,W.N., Lee,S.Y.
            and Choi,Y.
  TITLE     TRANCE is a novel ligand of the tumor necrosis factor receptor
            family that activates c-Jun N-terminal kinase in T cells
  JOURNAL   J. Biol. Chem. 272 (40), 25190-25194 (1997)
  MEDLINE   97460112
REFERENCE   2  (bases 1 to 2237)
  AUTHORS   Wong,B.R., Josien,R., Lee,S.Y., Sauter,B., Li,H.L., Steinman,R.M.
            and Choi,Y.
  TITLE     TRANCE (tumor necrosis factor [TNF]-related activation-induced
            cytokine), a new TNF family member predominantly expressed in T
            cells, is a dendritic cell-specific survival factor
  JOURNAL   J. Exp. Med. 186 (12), 2075-2080 (1997)
  MEDLINE   98060869
REFERENCE   3  (bases 1 to 2237)
  AUTHORS   Fuller,K., Wong,B., Fox,S., Choi,Y. and Chambers,T.J.
  TITLE     TRANCE is necessary and sufficient for osteoblast-mediated
            activation of bone resorption in osteoclasts
  JOURNAL   J. Exp. Med. 188 (5), 997-1001 (1998)
  MEDLINE   98401035
REFERENCE   4  (bases 1 to 2237)
  AUTHORS   Wong,B.R., Josien,R., Lee,S.Y., Vologodskaia,M., Steinman,R.M. and
            Choi,Y.
  TITLE     The TRAF family of signal transducers mediates NF-kappaB activati
            by the TRANCE receptor
  JOURNAL   J. Biol. Chem. 273 (43), 28355-28359 (1998)
  MEDLINE   98447691
REFERENCE   5  (bases 1 to 2237)
  AUTHORS   Wong,B.R., Rho,J., Arron,J., Lee,S.Y., Robinson,E. and Choi,Y.
  TITLE     Direct Submission
  JOURNAL   Submitted (09-JUL-1997) Howard Hughes Medical Institue, The
            Rockefeller University, 1230 York Ave., New York, NY 10021, USA
FEATURES             Location/Qualifiers
     source          1. .2237
                     /organism="Mus musculus"
                     /db_xref="taxon:10090"
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Sequence Comparison

D'